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Synthetic Organic Chemicals

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The Diels-Alder Diene Synthesis

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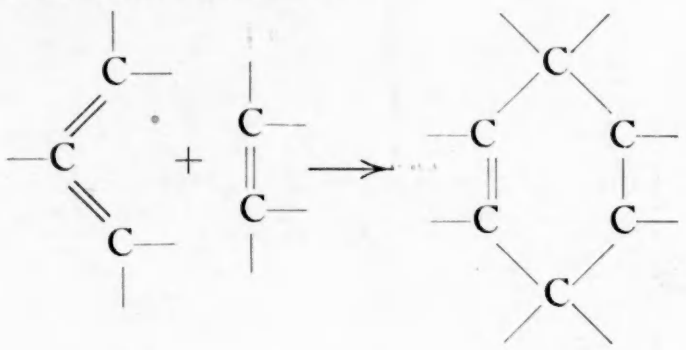
DISCOVERED about ten years ago by Diels and Alder, the diene synthesis has been developed by these workers and others into an extraordinarily useful and valuable tool of the organic chemist. The principle of the reaction is quite simple, and may be expressed by the following equation:



A B C

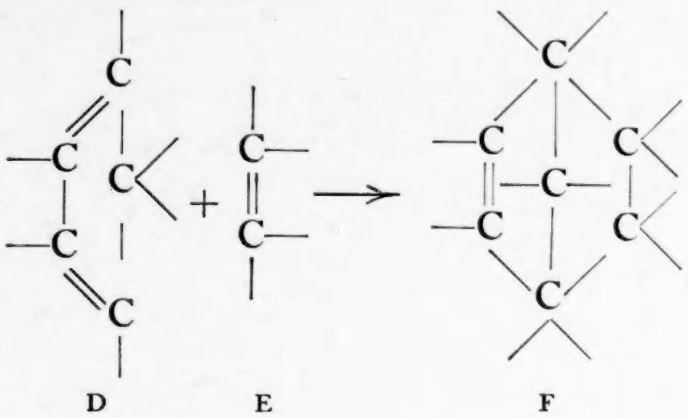
The diene, A, which must be a conjugated diene, unites with the olefine, B, under suitable conditions to form the cyclic derivative, C, which is generally referred to as the adduct.

Applicability

Wide variations in the reactants are possible. Thus, the conjugated diene, A, and the olefine, B, may be substituted by one or more groups in any of the possible positions. The different substituents introduced exert a strong influence on the relative ease with which the reaction occurs. Ordinarily, a carbonyl group, —CO—, attached to the double bond of the olefine, lends a marked speed of reaction to the system. Thus, the α,β-unsaturated aldehydes, such as acrolein, crotonaldehyde and cinnamaldehyde, and the α,β-unsaturated ketones, such as vinyl methyl ketone and the alkylidene acetones, as well as similarly unsaturated acids of the acrylic acid series, such as acrylic acid, methacrylic acid, and cinnamic acid, tend to react readily with many dienes. Even greater reactivity may be conferred on the olefine, B, by introducing two carbonyl groups symmetrically situated. Thus, maleic acid and quinone and their homologues and derivatives appear to react quite readily, often even at room temperatures or below. Acetylene dicarboxylic esters, as well as many other acetylenic derivatives, react in this synthesis to yield cyclic compounds with two instead of one double bond in the ring. Olefinic bonds between two nitrogen atoms, as in azodicarboxylic acid esters, also react to give pyridazine derivatives. Such a compound, namely, 3,3,5-trimethyl-Δ^4-tetrahydro-1,2-pyridazine-1,2-dicarboxylic acid diethyl ester, was one of the first substances prepared by Diels which aided in developing the concept of the diene synthesis. An interesting type of

olefine that may be used is the product of a previous diene synthesis.

The diene, in addition to being a simple, straight chain hydrocarbon, may be a cyclic compound, such as cyclopentadiene, cyclohexadiene, or even anthracene. In such cases, bicyclic derivatives result, as shown in the equation:



D E F

This variation permitted Diels and Alder to synthesize with extraordinary ease a number of otherwise difficultly accessible natural products of the camphor and terpene series, and led Alder into a study of the stereoisomerisms involved in these bicyclic systems. The diene, D, may also be heterocyclic, as, for example, furane, or a conjugated polyene containing more than two double bonds, such as a fulvene, or any of several highly unsaturated acids found in drying oils and fish oils. For each pair of conjugated double bonds one molecule of olefine reacts.

Benzenoid rings and thiophene rings appear to be inert. Heterocyclic nitrogen compounds, such as pyrrole, pyridine, and quinoline derivatives, react by a different mechanism to give a number of highly complex products, the structures of which have been difficult to determine exactly. Similarly, aromatic hydrazo compounds yield complicated adducts with interesting properties. Stable and unstable modifications and their rearrangement products are encountered in the reaction mixture.

Ordinarily, the reactants are mixed together in an inert solvent, such as ether, and allowed to stand for a day or so. Since the products in many cases are crystalline solids of lower solubility than the starting materials, the occurrence of a reaction is evidenced by a separation of the adduct in crystalline form. In some cases, as in the addition of maleic anhydride to 2,3-dimethylbutadiene, the reaction is so violent as to require considerable amounts of diluent. In other cases, however, refluxing is necessary, and a higher boiling solvent may be required. With a good many pairs of compounds, no reaction can be brought about even with long continued heating at elevated temperatures. Thus far, no general catalyst has been found, and in most cases none is necessary, but the development of a suitable catalytic agent would be valuable in that it would endow the synthesis with a greater field of application than it now possesses.

Uses of the Synthesis

The diene synthesis has proved valuable for many purposes in addition to its use in the synthesis and preparation of a number of complex cyclic. bicyclic, and polycyclic derivatives. One of the most important uses is in the determination of structure. Maleic anhydride is an especially valuable reagent for this purpose in that it may be employed quite generally to disclose the presence of a conjugated double bond system in a molecule. The structures of abietic acid, of α-phellandrene, and of various drying oils have been elucidated in this way. An important method of structure determination lies in observing the products of thermal decomposition of the adducts. Sometimes a retrograde diene synthesis occurs; in other cases the fragmentation proceeds differently. Definite conclusions as to structure may be drawn in many instances.

In analytical work, conjugated dienes often may be determined qualitatively,

and quantitatively by conversion into a diene adduct, usually with maleic anhydride. Thus, the simpler dienes found in gasoline may be removed and determined quantitatively by combination with maleic anhydride. The crystalline adducts formed have characteristic melting points. A further development of this analytical method was made by Windaus, who found that ergosterol derivatives react with varying degrees of ease, depending on the temperature of reaction. By arbitrary adjustment of the temperature, a diene fractionation can be carried out.

An interesting application which has attained some commercial importance depends on what may be considered a variation of the true diene synthesis. When maleic anhydride is mixed with an olefinic substance capable of polymerization, a co-polymerization often may be induced, giving long chain molecules in which maleic anhydride units probably alternate with units of the polymerizing olefine. Vinyl acetate and styrene are examples of olefines which undergo this multi-diene synthesis. The products have interesting possibilities as plastics. Other less complex adducts have been applied successfully in the resin field.

The diene synthesis has many other uses and applications which are described in the literature. As a matter of biological interest, it should be pointed out that the synthesis is one of the very few known reactions which occur under conditions suitable for utilization in plant or animal life. Of theoretical interest is the fact that the diene synthesis is exceptional among organic reactions for the reason that no inorganic substance need be present for its successful completion.

Eastman Organic Chemicals as Analytical Reagents

XLIV REAGENTS FOR ZINC

QUINALDINIC ACID

Ray and Majundar, Z. ANAL. CHEM., *100*, 324 (1934)

Ray and Bose, MIKROCHEMIE., *12*, 89 (1933)

In the presence of alkaline tartrate, only zinc precipitates with quinaldinic acid. To a sulfuric acid solution of the zinc is added nitric acid to oxidize any iron present. Rochelle salt and ammonium chloride then are introduced and the solution neutralized with ammonia, using a mixed indicator of methyl red and methylene blue. The solution is made alkaline with a slight excess of ammonia, diluted to 150 c.c., heated to 50° C., and then a solution of ammonium quinaldinate added dropwise in slight excess with constant stirring. The precipitate is filtered, washed, dried at 125° C., and weighed; it contains 15.29% zinc. Chromium interferes, apparently forming a soluble or colloidal zinc chromate.

METHYL RED

Tananaew and Georgobiani, Z. ANAL. CHEM., *107*, 92 (1936)

The zinc is converted to the sulfate and titrated in neutral solution with potassium ferrocyanide, using methyl red as an absorption indicator. The titration is carried out preferably at 60° to 70° C. The methyl red is adsorbed on the precipitate, with the formation of a rose color so long as there is no excess of ferrocyanide present. The color changes to yellow at the equivalent point. The best results are obtained by using .05 to 0.1 molar potassium ferrocyanide for titrating .01 to 0.1 molar zinc sulfate. Ferric ions and ammonium salts interfere.

Thirty-one New Eastman Organic Chemicals

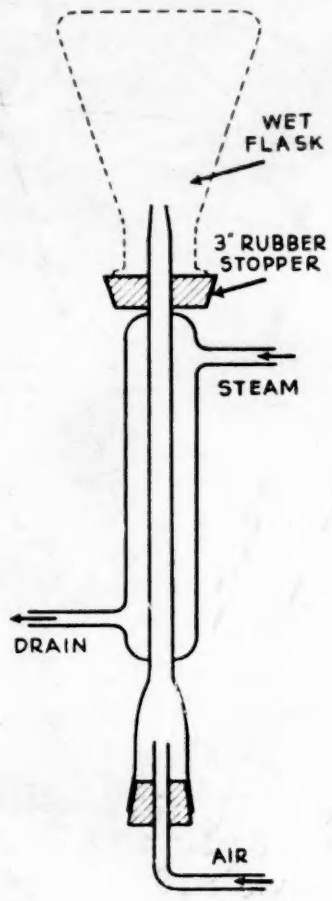
Since the publication of List No. 28, *Eastman Organic Chemicals*, the following thirty-one compounds have been added to our stock. Prices and purity specifications will be forwarded upon request.

P 4468	Aurin Tricarboxylic Acid Ammonium Salt (Pract.)
4486	Benzoyl Persulfide
3331	Benzyl Salicylate
4502	Chloroacetonitrile
T 4513	5-Chloro-2-aminobenzoic Acid (Techn.)
370	n-Decyl Alcohol (Primary)
4439	1,8-Diaminonaphthalene
4517	2,6-Dibromopyridine
T 4492	3,3-Dichlorobenzidine Sulfate (Techn.)
P 4484	2,5-Dimethoxyaniline (Pract.)
P 4556	α-Dimethylaminoglycerol (Pract.)
4477	p-Ethoxydiphenyl Sulfide
4544-X	2-Ethylhexyl Sebacate
P 4514	o-Ethylphenol (Pract.)
P 4520	m-Ethylphenol (Pract.)
P 4503	p-Ethylphenol (Pract.)
P 3658	n-Hexaldehyde (Pract.)
2773	Indole
4551	o-Iodobenzoyl Chloride
P 4555	α-Menthyl Benzoate (Pract.)
P 4528	Menthyl Salicylate (Pract.)
4343	Methyl Levulinate
T 4475	Morin (Techn.)
4483	Neocupferron
P 4485	2-Nitro-4-chlorotoluene (Pract.)
P 4490	2-Nitro-6-chlorotoluene (Pract.)
4478	iso-Pulegol
4427	Purpurin
T 4512	Sodium 2,7-Anthraquinonedisulfonate (Techn.)
P 2280	Tetrachlorohydroquinone (Pract.)
4476	Thiohydroquinone (Mono)

Apparatus Drier

The drying of laboratory glassware often is an annoying problem. A simple apparatus for this purpose which has proved very satisfactory is shown in the accompanying diagram. It supplies a stream of warm air blown directly into the equipment to be dried. It has the added advantage of being easy to construct from materials available in any laboratory.

An ordinary glass condenser serves as the heating unit for the air. If the inner tube is packed lightly (not tightly enough to interfere with the passage of the air) with steel wool, or, even better, with copper wool, more efficient heating will be obtained. Steam from an ordinary steam line is passed through the outer jacket, heating the inner tube and the packing. Any air tap may serve as a source for the air introduced at the bottom. However, care must be taken that the air pressure is not so great that the flask is blown from the stand. The rubber stopper on the condenser tube serves as a support for the glassware and minimizes danger of breakage.



Although the air does not become very hot in this apparatus, the rate of drying is considerably faster than when air is employed directly from a tap, and its use precludes fire hazard from electrically operated heaters.